

27. The pharmaceutical composition of claim 6, wherein R<sub>1</sub> is -CH<sub>2</sub>OH, G is -OCH<sub>3</sub>, and R<sub>3</sub> is 1,1-dimethyl heptyl.

28. The pharmaceutical composition of claim 27 wherein the dotted line represents a double bond.

29. The compound of claim 4 wherein the dotted line represents a double bond.

#### REMARKS

Claims 1-4, 6-8 and 17, as amended, and new claims 18-29 appear in this application for the Examiner's review and consideration. Claims 1 and 17 have been amended to recite a genus for the elected species. New claims 18-20 and 25-27 are copies of claims 2-4 but are dependent upon claims 6 or 17, respectively. New claims 22-25 are copies of claims 6-8 but are dependent upon claim 17. New claims 21, 28 and 29 are specifically directed to the elected species. As no new matter has been added, these claims should be entered at this time. A marked up copy of the claim amendments appears in Appendix A, while a listing of all current claims appears in Appendix B. These claims should be examined in the following order: 1-4, 28, 6-8, 25-27, and 17-24.

In response to the Examiner's restriction requirement, Applicants specifically elect the compound disclosed in the specification as being known as HU-308. The synthesis of this compound and its resulting structure are shown in Figure 1 and Example 3, while the unexpected advantages of this compound are described in Figures 2-4 and Examples 12-14. These unexpected advantages clearly support the patentability of the present claims.

No fee is believed to be due for this submission. Should any fees be due, however, please charge such fees to Winston & Strawn Deposit Account No. 501-814.

Date: 8/2/02

Respectfully submitted,



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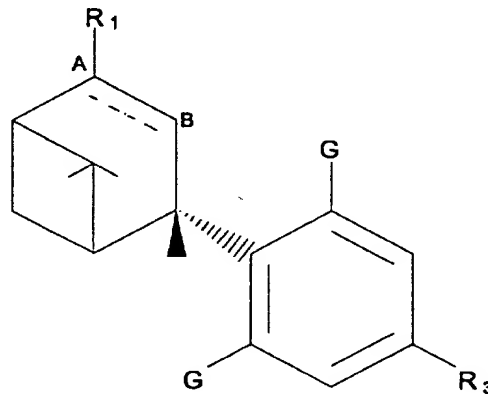
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## APPENDIX A

MARKED COPY OF AMENDED CLAIMS

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1. A [pharmaceutical composition for treating or preventing hypertension, inflammation, peripheral pain, gastrointestinal disorders, or autoimmune disease, comprising as an active ingredient a] compound of the general formula:



having the (3S,4S) configuration, and which is essentially free of the (3R,4R) enantiomer, wherein:

A---B designates an optional double bond,

R<sub>1</sub> is [(a) -R'N(R'')<sub>2</sub> wherein R' is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and each R'', which may be the same or different, is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl optionally containing a terminal -OR''' or -OC(O)R''' moiety wherein R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl, (b) -Q wherein Q is a heterocyclic moiety having a labile hydrogen atom so that said moiety acts as a carboxylic acid analogue, (c) -R'X wherein R' is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and X is halogen, (d) -R'C(O)N(R'')<sub>2</sub> wherein R' is a direct bond or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and each R'', which may be the same or different, is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl optionally containing a terminal -OR''' or -OC(O)R''' moiety wherein R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl, (e) -R'C(O)OR'' wherein R' is a direct bond or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and R'' is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl optionally containing a terminal -OR''' or -OC(O)R''' moiety wherein R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched

chain alkyl, (f) -R' wherein R' is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl, or (g)] -R'OR''' wherein R' is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> alkyl;

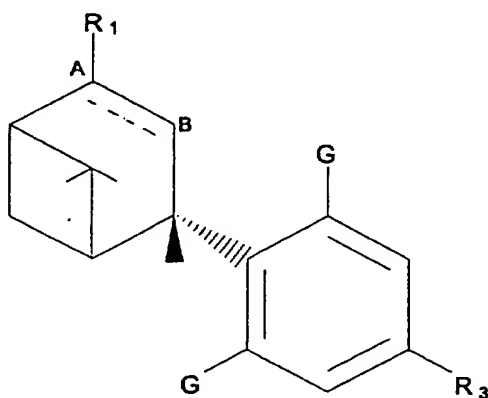
G is [hydrogen, halogen, or] -OR<sub>2</sub> wherein R<sub>2</sub> is [hydrogen or] C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl [optionally containing a terminal -OR''', -OC(O)R''', C(O)OR''', or -C(O)R'' moiety wherein R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl]; and

R<sub>3</sub> is [(a)] C<sub>1</sub>-C<sub>12</sub> straight or branched chain [alkyl, (b) -OR''', in which R''' is a straight chain or branched C<sub>2</sub>-C<sub>9</sub> alkyl which may be substituted at the terminal carbon atom by a phenyl group, or (c) -(CH<sub>2</sub>)<sub>n</sub> OR''' wherein n is an integer of 1 to 7 and R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub>] alkyl.

6. (amended) [A] The pharmaceutical composition for treating, preventing, or managing hypertension, inflammation, peripheral pain, gastrointestinal disorders, or autoimmune diseases comprising as an active ingredient a therapeutically effective amount of a compound of claim 1.

7. (amended) [A] The pharmaceutical composition of claim 6 further comprising a pharmaceutically acceptable diluent or carrier.

17. (amended) A CB2 specific agonist comprising a compound of the general formula:



having the (3S,4S) configuration, and which is essentially free of the (3R,4R) enantiomer, wherein:

A---B designates an optional double bond,

R<sub>1</sub> is [(a) -R'N(R'')<sub>2</sub> wherein R' is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and each R'', which may be the same or different, is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl optionally containing a terminal -OR''' or -OC(O)R''' moiety wherein R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl, (b) -Q wherein Q is a heterocyclic moiety having a labile hydrogen atom so that said moiety acts as a carboxylic acid analogue, (c) -R'X wherein R' is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and X is halogen, (d) -R'C(O)N(R'')<sub>2</sub> wherein R' is a direct bond or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and each R'', which may be the same or different, is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl optionally containing a terminal -OR''' or -OC(O)R''' moiety wherein R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl, (e) -R'C(O)OR'' wherein R' is a direct bond or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and R'' is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl optionally containing a terminal -OR''' or -OC(O)R''' moiety wherein R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl, (f) -R' wherein R' is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl, or (g)] -R'OR''' wherein R' is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> alkyl;

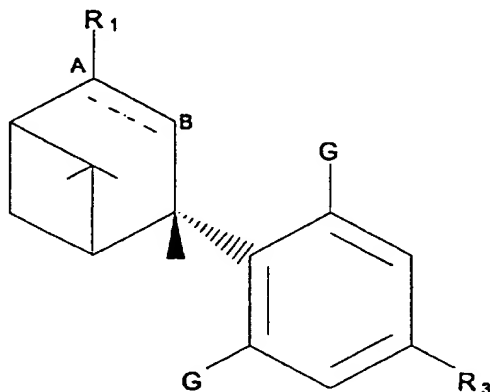
G is [hydrogen, halogen, or] -OR<sub>2</sub> wherein R<sub>2</sub> is [hydrogen or] C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl [optionally containing a terminal -OR''', -OC(O)R''', C(O)OR''', or -C(O)R'' moiety wherein R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl]; and

R<sub>3</sub> is [(a)] C<sub>1</sub>-C<sub>12</sub> straight or branched chain [alkyl, (b) -OR''', in which R''' is a straight chain or branched C<sub>2</sub>-C<sub>9</sub> alkyl which may be substituted at the terminal carbon atom by a phenyl group, or (c) -(CH<sub>2</sub>)<sub>n</sub> OR''' wherein n is an integer of 1 to 7 and R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> alkyl].



**APPENDIX B - CURRENTLY PENDING CLAIMS**

1. (amended) A compound of the general formula:



having the (3S,4S) configuration, and which is essentially free of the (3R,4R) enantiomer, wherein:

A---B designates an optional double bond,

R<sub>1</sub> is -R'OR''' wherein R' is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> alkyl;

G is -OR<sub>2</sub> wherein R<sub>2</sub> is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl; and

R<sub>3</sub> is C<sub>1</sub>-C<sub>12</sub> straight or branched chain alkyl.

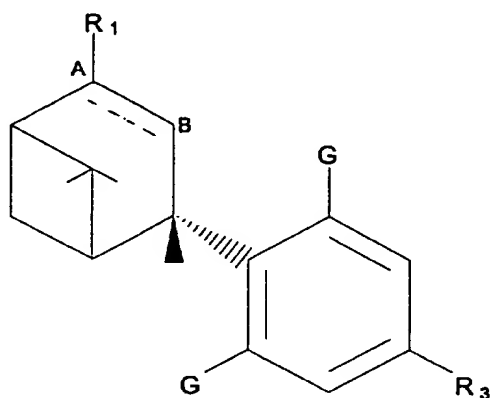
2. The compound of claim 1, wherein R<sub>3</sub> is a straight chain or branched -C<sub>5</sub>-C<sub>9</sub> alkyl.
3. The compound of claim 1, wherein R<sub>3</sub> is 1,1-dimethyl heptyl or 1,2-dimethyl heptyl.
4. The compound of claim 1, wherein R<sub>1</sub> is -CH<sub>2</sub>OH, G is -OCH<sub>3</sub>, and R<sub>3</sub> is 1,1-dimethyl heptyl.
5. cancelled

6. The pharmaceutical composition for treating, preventing, or managing hypertension, inflammation, peripheral pain, gastrointestinal disorders, or autoimmune diseases comprising as an active ingredient a therapeutically effective amount of a compound of claim 1.

7. The pharmaceutical composition of claim 6 further comprising a pharmaceutically acceptable diluent or carrier.

8. The pharmaceutical composition of claim 7, wherein the diluent is an aqueous cosolvent solution comprising a pharmaceutically acceptable cosolvent, a micellar solution or emulsion prepared with natural or synthetic ionic or non-ionic surfactants, or a combination of such cosolvent and micellar or emulsion solutions.

17. (amended) A CB2 specific agonist comprising a compound of the general formula:



having the (3S,4S) configuration, and which is essentially free of the (3R,4R) enantiomer, wherein:

A---B designates an optional double bond,

R<sub>1</sub> is -R'OR''' wherein R' is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl and R''' is hydrogen or C<sub>1</sub>-C<sub>5</sub> alkyl;

G is -OR<sub>2</sub> wherein R<sub>2</sub> is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl; and

R<sub>3</sub> is C<sub>1</sub>-C<sub>12</sub> straight or branched chain alkyl.

18. The agonist of claim 17, wherein  $R_3$  is a straight chain or branched  $-C_5-C_9$  alkyl.
19. The agonist of claim 17, wherein  $R_3$  is 1,1-dimethyl heptyl or 1,2-dimethyl heptyl.
20. The agonist of claim 17, wherein  $R_1$  is  $-CH_2OH$ ,  $G$  is  $-OCH_3$ , and  $R_3$  is 1,1-dimethyl heptyl.
21. The agonist of claim 20, wherein the dotted line represents a double bond.
22. A pharmaceutical composition for treating, preventing, or managing hypertension, inflammation, peripheral pain, gastrointestinal disorders, or autoimmune diseases comprising as an active ingredient a therapeutically effective amount of the CB2 specific agonist of claim 17.
23. A pharmaceutical composition of claim 22, further comprising a pharmaceutically acceptable diluent or carrier.
24. The pharmaceutical composition of claim 22, wherein the diluent is an aqueous cosolvent solution comprising a pharmaceutically acceptable cosolvent, a micellar solution or emulsion prepared with natural or synthetic ionic or non-ionic surfactants, or a combination of such cosolvent and micellar or emulsion solutions.
25. The pharmaceutical composition of claim 6, wherein  $R_3$  is a straight chain or branched  $-C_5-C_9$  alkyl.
26. The pharmaceutical composition of claim 6, wherein  $R_3$  is 1,1-dimethyl heptyl or 1,2-dimethyl heptyl.
27. The pharmaceutical composition of claim 6, wherein  $R_1$  is  $-CH_2OH$ ,  $G$  is  $-OCH_3$ , and  $R_3$  is 1,1-dimethyl heptyl.

28. The pharmaceutical composition of claim 27 wherein the dotted line represents a double bond.

29. The compound of claim 4 wherein the dotted line represents a double bond.